having adenine at the 11th position from its 5' end. We measured the ΔT_m (° C.) values are relative to control ODN22 essentially as described (Jones "JOC" 58:2983 1993). The results are shown in Table II.

TABLE II

Thermal Denaturation Data for 9-Modified Phenoxazine ODNs
Target DNA (33)/RNA (31): 5'-AAA-AAG-AGA-GGG-AGA (SEQ ID NO. 21, 22)
Target DNA (34)/RNA (32): 5'-AAA-AAG-AGA-GAG-AGA (SEQ ID NO. 23, 24)

ODN	test base	31	ΔTm*	32	ΔTm (31–32)	33	ΔTm*	34	ΔTm (33–34)
22	C (control)	61 5	—	42.5	19.0	50.5	—	32.0	18.5
23	D (control)	65 0	3.5	44.5	20.5	54.0	3.5	33.0	21.0
24	(60) (control)	66 5	5.0	50.0	16.5	57.0	6.5	44.5	12.5
25	(55)	73 5	12.0	56.0	17.5	63.5	13.0	44.0	19.0
26	(57)	77 5	16.0	52.0	25.5	68.5	18.5	43.0	25.5
27	(59)	74.0	12.5	51.0	23.0	—	—	—	—
28	(58)	73 5	12.0	52.5	21.0	—	—	—	—
29	(61)	70 5	9.0	55.0	15.5	—	—	—	—
30	(65)	61 5	0	44.0	17.5	—	—	—	—

*DTm relative to ODN22.

This data demonstrates the enhancement in melting point afforded by oligonucleotides containing invention bases. The increased ΔTm(31–32) and ΔTm(33–34) values obtained with invention bases (57), (58) and (59) indicate that these invention bases have an increased binding specificity compared to 5-methylcytosine or 5-(1-propynyl) cytosine.

EXAMPLE 5

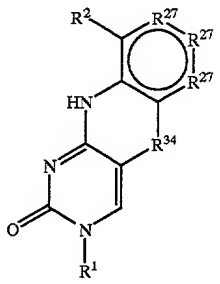
Increased potency of gene expression inhibition. We made a 20-mer phosphorothioate-linked DNA oligonucleotide, 5' TCC-CGC-XTG-TGA-CAT-CGA-TT 3' (SEQ ID NO. 25), where X was a structure (57) base. The oligonucleotide was complementary to the 3' untranslated region of the c-raf mRNA. A control oligonucleotide had the same sequence except that the X base was replaced with cytosine. Each oligonucleotide was tested to determine its potency at inhibiting expression c-raf gene expression essentially as described (Monia "Nature Med" 2:668–675 1966, WO 97/32604). Briefly, a range of concentrations of each oligonucleotide was transfected into A549 small lung carcinoma cells on two consecutive days, followed by preparing cell extracts 48 hours after the first transfection. Immunoblot assay for c-raf protein expression showed the control oligonucleotide reduced c-raf protein expression with an IC_{50} of about 20 nM. The test oligonucleotide containing the structure (57) base in place of cytosine was at least 20-fold more potent and had an IC_{50} of less than 1 nM.

Similar assays using an oligonucleotide containing about 8–18 bases that are complementary to raf or c-raf, e.g., the oligonucleotide sequence used in this example or a shortened version thereof, is accomplished in a similar manner using invention oligonucleotides containing 1, 2 or 3 invention bases having an R^2 moiety that increases binding affinity compared to a control oligonucleotide containing cytosine.

We claim:

1. A compound having the structure (1):

(1)

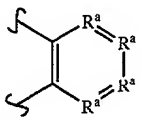


and tautomers, solvates and salts thereof, wherein

R^1 is an oligonucleotide, a protecting group, a linker or —H;

R^2 is $A(Z)_{X1}$, wherein A is a spacer and Z independently is a label bonding group optionally bonded to a detectable label, but R^2 is not amine, protected amine, nitro or cyano;

R^{27} is independently —CH═, —N═, —C(C_1–C_8 alkyl)═ or —C(halogen)═, but no adjacent R^{27} are both —N═, or two adjacent R^{27} are taken together to form a ring having the structure,



where R^a is independently —CH═, —N═, —C(C_{1-8} alkyl)═ or —C(halogen)═, but no adjacent R^a are both —N═;

R^{34} is —O—, —S— or —N(CH_3)—; and

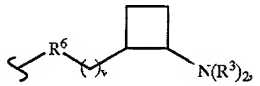
X1 is 1, 2 or 3.

2. The compound of claim 1 wherein R^2 is —R^{2C}—R^{2D}, wherein R^{2C} is a short spacer chain and R^{2D} is a hydrogen bond donor moiety or a moiety having a net positive charge of at least about +0.5 at pH 6–8 in aqueous solutions.

3. The compound of claim 1 wherein R^2 is $—R^6—(CH_2)_tNR^5C(NR^5)(NR^3)_2$, $—R^6—CH_2—CHR^{31}—N(R^3)_2$, $—R^6—(R^7)_v—N(R^3)_2$, $—R^6—(CH_2)_t—N(R^3)_2$, $—(CH_2)_{1-2}—O—(CH_2)_t—N(R^3)_2$,

(40)

(41)



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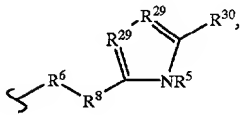

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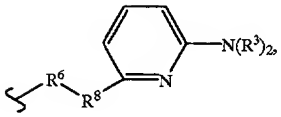

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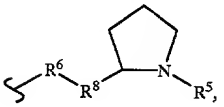

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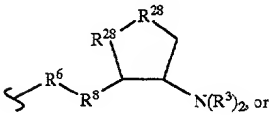

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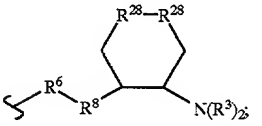
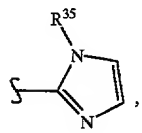


R^3 is independently —H, $—CH_3$, $—CH_2CH_3$, $—(CH_2)_w—N(R^{33})_2$ or a protecting group, or both R^3 together are a protecting group, or when R^2 is $—R^6—(CH_2)_t—N(R^3)_2$, one R^3 is —H, $—CH_3$, $—CH_2CH_3$, a protecting group or $—(CH_2)_w—N(R^{33})_2$ and the other R^3 is —H, $—CH_3$, $—CH_2CH_3$, $—(CH_2)_w—N(R^{33})_2$, $—CH(N[R^{33}]_2)—N(R^{33})_2$,

(48)



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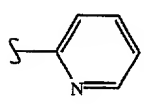
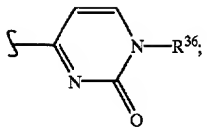


, or

(50)



R^5 is independently H or a protecting group;

R^6 is independently —S—, $—NR^5—$, —O— or $—CH_2—$;

R^7 is independently linear alkyl having 1, 2, 3 or 4 carbon atoms optionally substituted with one $—CH═CH—$, $—C≡C—$ or $—CH_2—O—CH_2—$ moiety, or R^7 is cyclic alkyl having 3, 4 or 5 carbon atoms, wherein one of the linear alkyl carbon atoms is optionally substituted with a single $—CH_3$, —CN, =O, —OH or protected hydroxyl, provided that the carbon atoms in any $—CH═CH—$ or $—CH_2—O—CH_2—$ moiety are not substituted with =O, —OH or protected hydroxyl;

R^8 is linear alkylene having 1 or 2 carbon atoms wherein one alkylene carbon atom is optionally substituted with a single $—CH_3$, —CN, =O, —OH or protected hydroxyl, or R^8 is absent;

R^{28} is independently $—CH_2—$, $—CH(CH_3)—$, $—CH(OCH_3)—$, $—CH(OR^5)—$ or —O—, but both are not —O—;

R^{29} is independently —N—, $—N(CH_3)—$, —CH—, $—C(CH_3)—$, but both are not $—N(CH_3)—$;

R^{30} is —H or $—N(R^3)_2$;

R^{31} is the side chain of an amino acid;

R^{33} is independently —H, $—CH_3$, $—CH_2CH_3$ or a protecting group;

R^{35} is H, C_1–C_4 alkyl or a protecting group;

R^{36} is —H, $—CH_3$, $—CH_2CH_3$, a protecting group or an optionally protected monosaccharide;

t is 1, 2, 3 or 4, but when R^6 is —O—, —S— or $—NR^5—$, t is 2, 3 or 4;

v is independently 0, 1 or 2; and

w is independently 1 or 2.

4. The compound of claim 3 wherein R^2 is $—CH_2—(CH_2)_tN(R^3)_2$, $—NR^5—(CH_2)_tN(R^3)_2$, $—S—(CH_2)_tN(R^3)_2$, $—O—(CH_2)_tN(R^3)_2$, $—O—(CH_2)_tNR^5C(NR^5)(NR^3)_2$, $—(CH_2)_{1-2}—O—(CH_2)_tN(R^3)_2$, $—R^6—CH_2—CHR^{31}—N(R^3)_2$, $—R^6—(R^7)_v—N(R^3)_2$, $—R^6—(CH_2)_t—NR^5C(NR^5)(NR^3)_2$, or $—CH_2(CH_2)_tNR^5C(NR^5)(NR^3)_2$.

5. The compound of claim 4 wherein t is 2.

6. The compound of claim 5 wherein R^3 independently is —H, $—CH_3$ $—C_2H_5$ or a protecting group.

7. The compound of claim 6 wherein R^2 is $—O—(CH_2)_2—NH_2$, $—O—(CH_2)_3—NH_2$, $—O—(CH_2)_2—N(CH_3)_2$, $—O—(CH_2)_3—N(CH_3)_2$, $—O—(CH_2)_2—NHCH_3$, $—O—(CH_2)_3—NHCH_3$, $—O—CH_2—CH(CH_3)—NH_2$, $—CH_2—O—(CH_2)_2—NH_2$, $—CH_2—O—(CH_2)_3—NH_2$ or $—(CH_2)_2—O—(CH_2)_2—NH_2$.

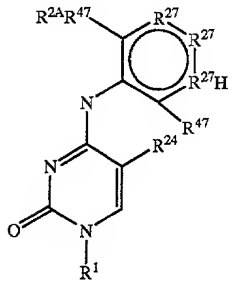
8. The compound of claim 3 wherein t is 2 or 3.

9. The compound of claim 1 wherein R^1 comprises —H, an optionally protected monosaccharide, hydroxyl, phosphate or hydrogen phosphonate.

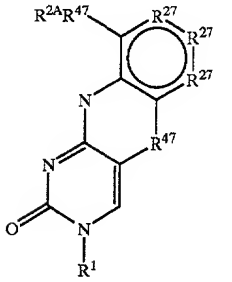
10. The compound of claim 1 wherein R^1 is optionally protected 2'-deoxy-R^{21}-substituted ribose, 2'-deoxyribose or ribose, wherein R^{21} is H, —OH, halogen or a moiety that enhances the nuclease stability of an oligonucleotide containing the optionally protected 2'-deoxy-R^{21}-substituted ribose, 2'-deoxyribose or ribose.

11. The compound of claim 1 having the structure designated by the numbers selected from the group consisting of (104), (105), (133), (134), (111), (112), (113), (115), (135), (136), (137), (138), (139), (120), (121), (121A), (143), (122), (123), (125), or (126):

(104)



(105)



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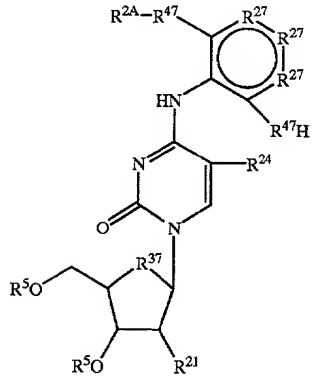

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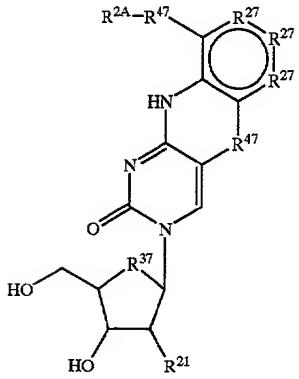

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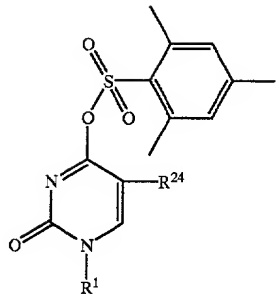
(111)



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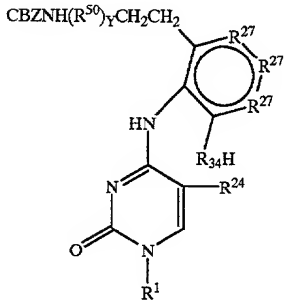

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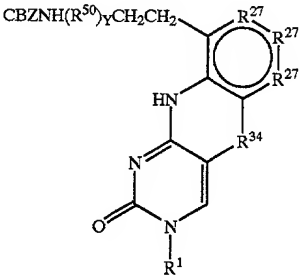

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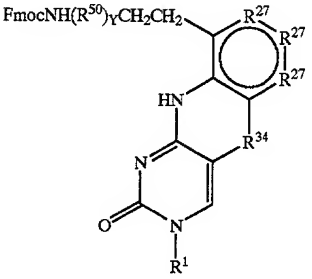

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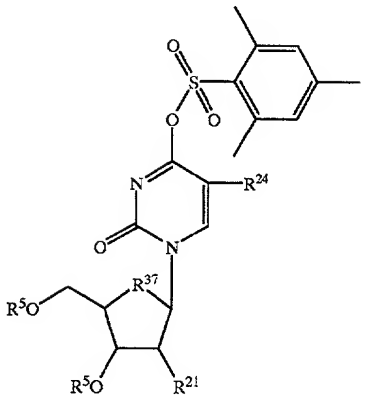

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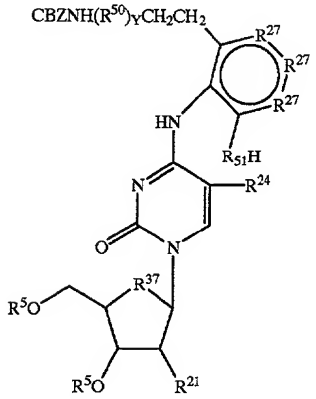

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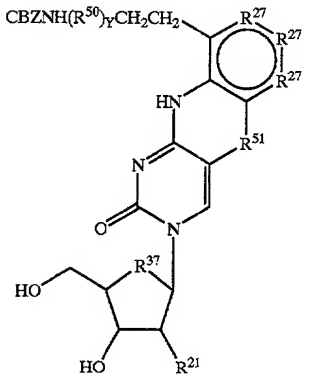

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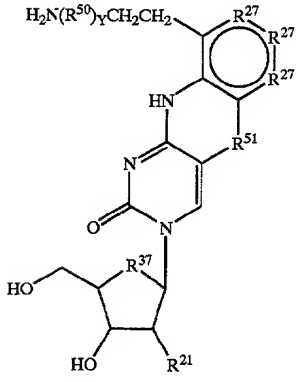

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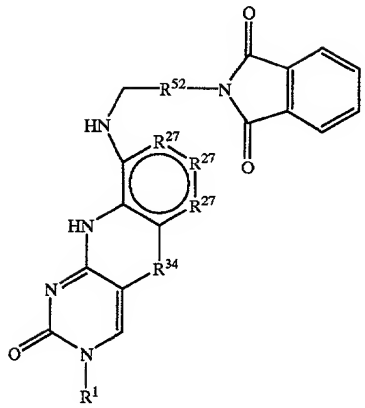

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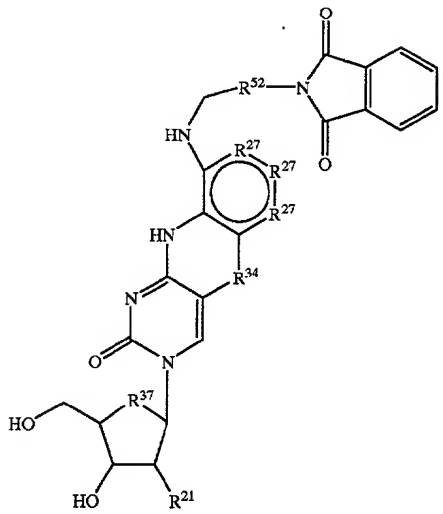

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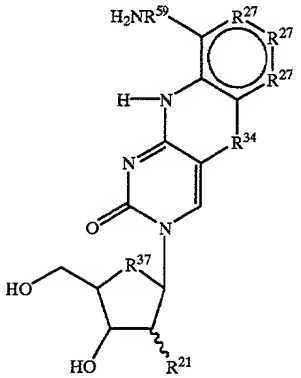

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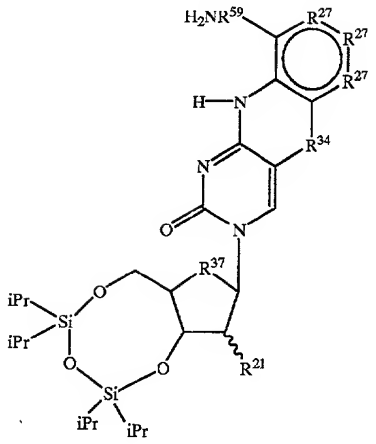
(123)



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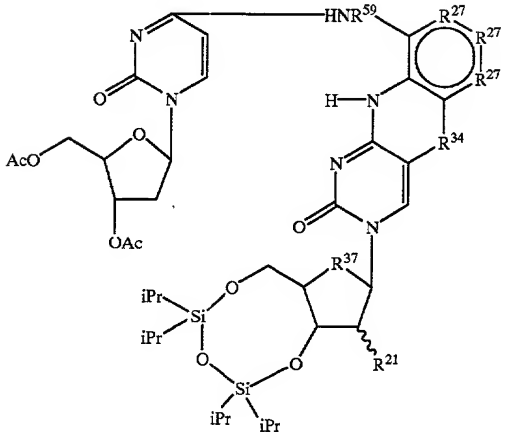

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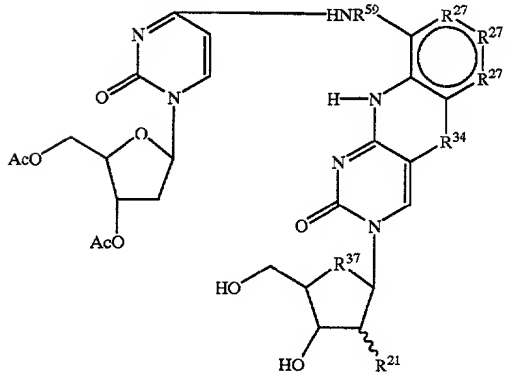


wherein

R^1 is an optionally protected monosaccharide;

R^{2A} is —OH;

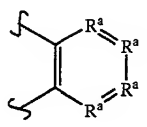
R^5 is independently —H or a protecting group;

R^6 is —O—, —S—, —NH— or —CH_2—,

R^{21} is H, —OH, halogen or a moiety that enhances the nuclease stability of an oligonucleotide;

R^{24} is a halogen;

R^{27} is independently —CH═, —N═, —C(C_1–C_8 alkyl)═ or —C(halogen ═, but no adjacent R^{27} are both —N═, or two adjacent R^{27} are taken together to form a ring having the structure,



where R^a is independently —CH═, —N═, —C(C_{1-8} alkyl)═ or —C(halogen)═, but no adjacent R^a are both —N═;

R^{34} is —O—, —S— or —N(CH_3)—;

R^{37} is —O—, —CH_2— or —CF_2—;

R^{47} is —O— or —S—;

R^{50} is —CH_2—, —C(O)—, —$(CH_2)_2$—O—$(CH_2)_2$—, —$(CH_2)_2$—NR^5—$(CH_2)_2$—, —$(CH_2)_2$—S—$(CH_2)_2$—, —CH($N(R^5)_2$)—, —CH($COOR^5$)— or —$C(CH_3)$—, —$C(C_2C_5)$— but adjacent moieties are not C(O);

R^{52} is —(CHR^{52A})—(R^{52B})—CHR^{52A}—, —CHR^{52A}—O—CHR^{52A}—, —CHR^{52A}—S—CHR^{52A}—, —CHR^{52A}—NR^5—CHR^{52}A—, C_1–C_{10} alkylene optionally substituted with 1 or 2 moieties selected from the group consisting of C_1–C_6 alkyl, —OR^5, ═O, —NO_2, —N_3, —CN, —$COOR^5$, or —$N(R^5)_2$, wherein any heteroatom is separated from the nitrogen atoms that R^{52} is linked to by one methylene and one or more —CHR^{52A}—;

R^{52A} is —H or C_1–C_6 alkyl;

R^{52B} is a bond;

R^{59} is —R^6—R^{60}—;

R^{60} is —$(CH_2)_{Z3}$—$(R^{61})_{Z1}$—$(CH_2)_{Z2}$—;

R^{61} is —O—, —S—, —NR^5—, —C(O)—, —CH_2—O—CH_2—, —CH_2—NR^5—CH_2— or CH_2—S—CH_2—;

Z1 is 0 or 1;

Z2 is 1, 2 or 3;

Z3 is 1, 2 or 3;

Y is 1, 2, 3 or 4;

CBZ is carboxybenzoyl;

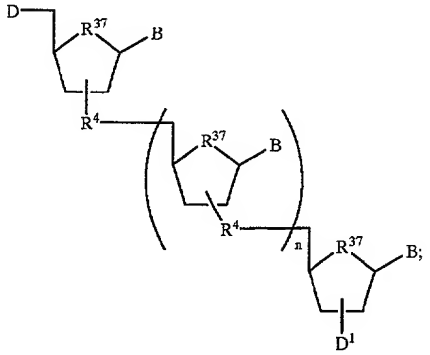
Fmoc is 9-fluorenylmethoxycarbonyl;

iPr is isopropyl; and

Ac is acetyl.

12. The compound of claim 1 wherein R^1 is an oligonucleotide having the structure (2):

(2)



wherein

D is —OH, protected —OH, an oligonucleotide coupling group or a solid support;

D^1 is an oligonucleotide coupling group, —OH, protected —OH or a solid support, wherein D^1 is bonded to one 2' or 3' position in the oligonucleotide of structure (2) and the adjacent 2' or 3' position in structure (2) is substituted with R^{21}, provided that D and D^1 are not both an oligonucleoide coupling group or they are not both a solid support;

R^4 is independently a phosphodiester linkage or a phosphodiester substitute linkage, wherein R^4 is bonded to one 2' or 3' position in the structure (2) oligonucleotide and the adjacent 2' or 3' position in structure (2) is substituted with R^{21};

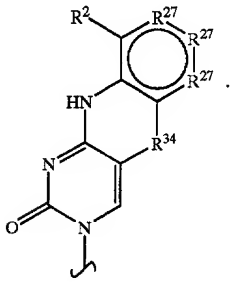
R^{21} is independently —H, —OH, halogen or a moiety that enhances the oligonucleotide against nuclease cleavage;

R^{37} is independently —O—, —CH_2—, —CF_2—;

n is an integer from 0 to 98; and

B independently is a purine or pyrimidine base or a protected derivative thereof, provided that at least one B is a base of structure (3)

(3)

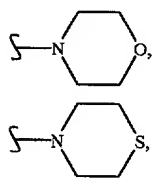


13. The compound of claim **12** wherein R^4 is independently 3'-O—P(S)(S)—O-5', 3'-O—P(S)(O)—O-5', 3'-O—P(O)(O)—O-5', 3'-O—P(Me)(O)—O-5', 3'-NH—P(O)(O)—O-5', 3'-S—CH_2—O-5', 2'-S—CH_2—O-5', 3'-O—CH_2—O-5', 2'-O—CH_2—O-5', 3'O—P(Me)(S)—O-5', 3'-CH_2—N(CH_3)—O-5', 2'-CH_2—N(CH_3)—O-5', or 3'-R^{38}—$P(N_2)$(O)—O-5', wherein

R^{38} independently is —O—, —CH_2— or —NH—;

R^{39} is a protecting group;

R^{40} independently is hydrogen, a protecting group, C_1–C_{12} alkyl optionally substituted with one, or two —O—, —C(O)—, —OC(O)—, —C(O)O—, —OR^{42}, —SR^{43}, —C(O)NR^{39}—, —C(O)$N(R^{41})_2$, —NR^{41}—, —$N(R^{41})_2$, halo, —CN, or —NO_2 moieties, or both R^{40} together with the nitrogen atom to which they are attached form



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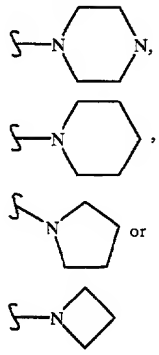
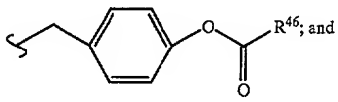


or both R^{40} together are a protecting group;

R^{41} independently is hydrogen, a protecting group, alkyl (C_1–C_4 or both R^{41} together are a protecting group;

R^{42} is hydrogen or a protecting group;

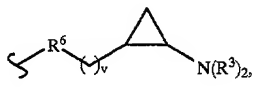
R^{43} is C_{1-6} alkyl or a protecting group; and R^{45} is —H, a counter ion or



R^{46} is alkyl containing 1–8 carbon atoms.

14. The compound of claim **12** wherein R^2 is —R^6—$(CH_2)_t$$NR^5$C($NR^5$)($NR^3$)$_2$, —$R^6$—$CH_2$—$CHR^{31}$—$N(R^3)_2$, —$R^6$—$(R^7)_v$—$N(R^3)_2$, —$R^6$—$(CH_2)_t$—$N(R^3)_2$, —$(CH_2)_{1-2}$—O—$(CH_2)_t$—$N(R^3)_2$,

(40)



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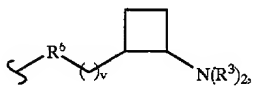

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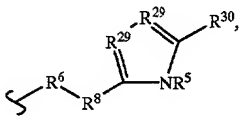

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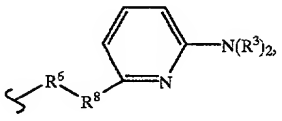

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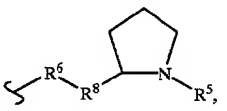

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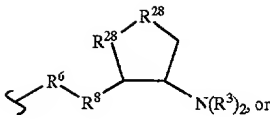

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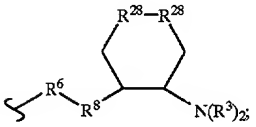
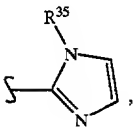


R^3 is independently —H, —CH_3, —CH_2CH_3, —$(CH_2)_w$—$N(R^{33})_2$ or a protecting group, or both R^3 together are a protecting group, or when R^2 is —R^6—$(CH_2)_t$—$N(R^3)_2$, one R^3 is —H, —CH_2CH_3, a protecting group or —$(CH_2)_w$—$N(R^{33})_2$ and the other R^3 is —H, —CH_3, —CH_2CH_3, —$(CH_2)_w$—$N(R^{33})_2$, —CH$(N[R^{33}]_2)$—$N(R^{33})_2$,

(48)



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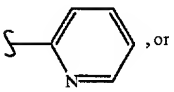

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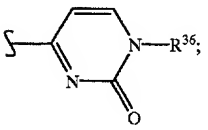


R^5 is independently H or a protecting group;

R^6 is independently —S—, —NR^5—, —O— or —CH_2—;

R^7 is independently linear alkyl having 1, 2, 3 or 4 carbon atoms optionally substituted with one —CH=CH—, —C≡C— or —CH_2—O—CH_2— moiety, or R^7 is cyclic alkyl having 3, 4 or 5 carbon atoms, wherein one of the linear alkyl carbon atoms is optionally substituted with a single —CH_3, —CN, =O, —OH or protected hydroxyl, provided that the carbon atoms in any —CH=CH— or —CH_2—O—CH_2— moiety are not substituted with =O, —OH or protected hydroxyl;

R^8 is linear alkylene having 1 or 2 carbon atoms wherein one alkylene carbon atom is optionally substituted with a single —CH_3, —CN, =O, —OH or protected hydroxyl, or R^8 is absent;

R^{28} is independently —CH_2—, —$CH(CH_3)$—, —CH(OCH_3)—, —CH(OR^5)— or —O—, but both are not —O—;

R^{29} is independently —N—, —$N(CH_3)$—, —CH—, —$C(CH_3)$—, but both are not —$N(CH_3)$—;

R^{30} is —H or —$N(R^3)_2$;

R^{31} is the side chain of an amino acid;

R^{33} is independently —H, —CH_3, —CH_2CH_3 or a protecting group;

R^{35} is H, C_1–C_4 alkyl or a protecting group;

R^{36} is —H, —CH_3, —CH_2CH_3, a protecting group or an optionally protected monosaccharide;

t is 1, 2, 3 or 4, but when R^6 is —O—, —S— or —NR^5—, t is 2, 3 or 4;

v is independently 0, 1 or 2; and

w is independently 1 or 2.

15. The compound of claim **14** wherein R^2 is —CH_2—$(CH_2)_tN(R^3)_2$, —NR^5—$(CH_2)_tN(R^3)_2$, —S—$(CH_2)_tN(R^3)_2$, —O—$(CH_2)_tN(R^3)_2$, —O—$(CH_2)_tNR^5C(NR^5)(NR^3)_2$, —$(CH_2)_{1-2}$—O—$(CH_2)_tN(R^3)_2$, —$R^6$—$CH_2$—$CHR^{31}$—$N(R^3)_2$, —$R^6$—$(R^7)_v$—$N(R^3)_2$, —$R^6$—$(CH_2)_t$—$NR^5C(NR^5)(NR^3)_2$, or —$CH_2(CH_2)_tNR^5C(NR^5)(NR^3)_2$.

16. The compound of claim **15** wherein t is 2 or 3.

17. The compound of claim **16** wherein R^3 independently is —H, —CH_3, —C_2H_5 or a protecting group.

18. The compound of claim **17** wherein R^2 is —O—$(CH_2)_2$—NH_2, —O—$(CH_2)_3$—NH_2, —O—$(CH_2)_2$—$N(CH_3)_2$, —O—$(CH_2)_3$—$N(CH_3)_2$, —O—$(CH_2)_2$—$NHCH_3$, —O—$(CH_2)_3$—$NHCH_3$, —O—CH_2—$CH(CH_3)$—NH_2, —CH_2—O—$(CH_2)_2$—NH_2, —CH_2—O—$(CH_2)_3$—NH_2 or —$(CH_2)_2$—O—$(CH_2)_2$—NH_2.

19. The compound of claim **12** wherein R^{21} is independently —H, —OH, halogen, protected hydroxyl, —O-methyl, —O-ethyl, —O-n-propyl, —O-allyl, —O—$(CH_2)_2OH$, —O—$(CH_2)_3OH$, —O—$(CH_2)_2F$, —O—$(CH_2)_sR^{65}$, —O—$(CH_2)_2$—$[O$—$(CH_2)_2]_rR^{65}$, —O—$(CH_2)_r$—O—$(CH_2)_r$—O—$(CH_2)_r$—R^{65}), —NH-methyl, —NH-ethyl, —NH-n-propyl, —NH—$(CH_2)_2OH$, —NH—$(CH_2)_3OH$, —NH—$(CH_2)_sR^{65}$, —S-methyl, —S-ethyl, —S-n-propyl, —S-allyl, —S—$(CH_2)_2OH$, —S—$(CH_2)_3OH$ —S—$(CH_2)_2F$, —S—$(CH_2)_sR^{65}$, or —S—$(CH_2)_2$—$[O$—$(CH_2)_2]_rR^{65}$, wherein

R^{65} is —H, —F, —OH, —OCH_3, —NH_2, —SH, protected hydroxyl, protected amino or protected thiol;

r is 1, 2, 3 or 4; and

s is 2, 3, 4, 5, 6, 7 or 8.

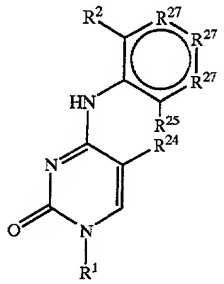
20. The compound of claim **19** wherein R^{21} is independently —H, —OH, —F, protected hydroxyl, —OCH_3, —O—CH_2CH_3, —O—CH_2CH_2OH, —O—CH_2CH_2F, —O—$CH_2CH_2CH_3$, —O—$CH_2CH_2CH_2OH$, —O—$CH_2CH_2CH_2F$, —O—CH_2CF_2H, —O—CH_2CF_3 or —O—CH_2CH_2—O—CH_3.

21. The compound of claim **12** wherein B independently are selected from the group consisting of a base of structure (3), guanosine, adenine, thymine, uracil, cytosine, 5-methylcytosine, 5-(1-propynyl)uracil, 5-(1-propynyl) cytosine, 5-(1-butynyl)uracil therefor 5-(1-butynyl)cytosine.

22. The compound of claim **12** wherein D^1 is H-phosphonate, a methylphosphonamidite, a β-cyanoethylphosphoramidite or a phosphoramidite.

23. A compound having the structure (4)

(4)



and tautomers, solvates and salts thereof wherein,

R^1, R^2 and R^{27} have the meanings given in claim 1;

R^{24} is a halogen;

R^{25} is —SH, —OH, ═S or ═O.

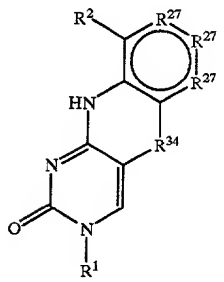
24. The compound of claim 23 wherein R^1 is —H or an optionally protected monosaccharide.

25. The compound of claim 24 wherein the optionally protected monosaccharide is 2'-deoxy-R^{21}-substituted ribose, wherein R^{21} is H, —OH, halogen or a moiety that enhances the nuclease stability of an oligonucleotide containing the optionally protected 2'-deoxy-R^{21}-substituted ribose, 2'-deoxyribose or ribose.

26. The compound of claim 25 wherein R^{21} is —H, —OH, —F, protected hydroxyl, —OCH_3, —O—CH_2CH_3, —O—CH_2CH_2OH, —O—CH_2CH_2F, —O—$CH_2CH_2CH_3$, —O—$CH_2CH_2CH_2OH$, —O—$CH_2CH_2CH_2F$, —O—CH_2CF_2H, —O—CH_2CF_3 or —O—CH_2CH_2—O—CH_3.

27. The compound of claim 1 having the structure (1):

(1)



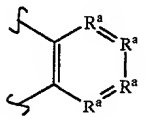
and tautomers, solvates and salts thereof, wherein

R^1 is a protecting group, an oligonucleotide, a nucleic acid, a polysaccharide, an optionally protected monosaccharide, hydroxyl, phosphate, hydrogen phosphonate, halo, azido, protected hydroxyl, or —H;

R^2 is $A(Z)_{X1}$, but R^2 is not amine, protected amine, nitro or cyano;

R^5 is H or a protecting group;

R^{27} is independently —CH═, —N═, —C(C_1–C_8 alkyl)═ or —C(halogen)═, but no adjacent R^{27} are both —N═, or two adjacent R^{27} are taken together to form a ring having the structure,



;

R^{34} is —O—, —S— or —$N(CH_3)$—;

R^a is independently —CH═, —N═, —C(C_{1-8} alkyl)═ or —C(halogen)═, but no adjacent R^a are both —N═;

A is a backbone chain of 2–16 carbon atoms, any 1, 2 or 3 of which are optionally replaced with N, O or S atoms, wherein the backbone chain is optionally substituted independently with 1, 2 or 3 of the following: C_1–C_8 alkyl, —OR^5, ═O, —NO_2, —N_3, —$COOR^5$, —$N(R^5)_2$, or —CN groups, C_1–C_8 alkyl substituted with —OH, ═O, —NO_2, —N_3, —$COOR^5$, —$N(R^5)_2$, or —CN groups, or any of the foregoing in which —CH_2— is replaced with —O—, —NH— or —N(C_1–C_8 alkyl);

X1 is 1, 2 or 3;

Y is H, 2-hydroxypyridine, N-hydroxysuccinimide, p-nitrophenyl, acylimidazole, maleimide, trifluoroacetate, an imido, a sulfonate, an imine 1,2-cyclohexanedione, glyoxal or an alpha-halo ketone; and

Z independently is —NH_2, —CHO, —SH, —CO_2Y, OY.

28. The compound of claim 27 wherein Z is bonded to a detectable label.

29. The compound of claim 27 wherein R^1 is an oligonucleotide.

30. The compound of claim 27 wherein R^1 is an optionally protected monosaccharide.

* * * * *